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Retrospective Study

Outcomes of high-grade aneurysmal subarachnoid hemorrhage patients treated with coiling and ventricular intracranial pressure monitoring

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Abstract

BACKGROUND

High-grade aneurysmal subarachnoid hemorrhage is a devastating disease with a low favorable outcome. Elevated intracranial pressure is a substantial feature of high-grade aneurysmal subarachnoid hemorrhage that can result to secondary brain injury. Early control of intracranial pressure including decompressive craniectomy and external ventricular drainage had been reported to be associated with improved outcomes. But in recent years, little is known whether external ventricular drainage and intracranial pressure monitoring after coiling could improve outcomes in high-grade aneurysmal subarachnoid hemorrhage.

AIM

To investigate the outcomes of high-grade aneurysmal subarachnoid hemorrhage patients with coiling and ventricular intracranial pressure monitoring.

METHODS

A retrospective analysis of a consecutive series of high-grade patients treated between Jan 2016 and Jun 2017 was performed. In our center, followed by continuous intracranial pressure monitoring, the use of ventricular pressure probe for endovascular coiling and invasive intracranial pressure monitoring in the acute phase is considered to be the first choice for the treatment of high-grade patients. We retrospectively analyzed patient characteristics, radiological features, intracranial pressure monitoring parameters, complications, mortality and outcome.

conflict of interest.

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RESULTS

A total of 36 patients were included, and 32 (88.89%) survived. The overall mortality rate was 11.11%. No patient suffered from aneurysm re-rupture. The intracranial pressure in 33 patients (91.67%) was maintained within the normal range by ventricular drainage during the treatment. A favorable outcome was achieved in 18 patients (50%) with 6 mo follow-up. Delayed cerebral ischemia and Glasgow coma scale were considered as significant predictors of outcome (2.066 and -0.296, respectively, $P < 0.05$).

CONCLUSION

Ventricular intracranial pressure monitoring may effectively maintain the intracranial pressure within the normal range. Despite the small number of cases in the current work, high-grade patients may benefit from a combination therapy of early coiling and subsequent ventricular intracranial pressure monitoring.

Key Words: Subarachnoid hemorrhage; High-grade; Outcome; Ventricular drainage; Intracranial pressure

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Core Tip: Ventricular intracranial pressure monitoring may effectively maintain the intracranial pressure within the normal range. Intractable intracranial hypertension in high-grade aneurysmal subarachnoid hemorrhage patients could be managed through external ventricular drainage and intracranial pressure monitoring. Combination therapy of early endovascular coiling followed by external ventricular drainage and intracranial pressure monitoring may also be suitable for high-grade aneurysmal subarachnoid hemorrhage patients.

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INTRODUCTION

High-grade (World Federation of Neurosurgical Societies (WFNS) Grades IV and V) aneurysmal subarachnoid hemorrhage (aSAH) is regarded as a devastating disease with high mortality (23%-75%) and a low favorable outcome (22%-56%)[1-4]. The re-rupture rate of the aneurysm is high: 15% in the first 24 h, showing correlation with high mortality (70%). Early aggressive surgery including clipping and coiling was well accepted.

Though the mortality decreased, functional outcomes of high-grade patients do not make significant improvements[1,2,5]. Elevated intracranial pressure (ICP) is a substantial feature of high-grade aSAH[6]. Several factors, such as early brain injury, global cerebral edema and hydrocephalus contribute to the development of intracranial hypertension, further leading to decreased cerebral perfusion pressure (CPP), cerebral ischemia and a poor outcome[7,8]. Therefore, strategies to control ICP and maintain optimal CPP play the critical role in the following management of high-grade patients. Though microsurgery could maintain ICP within a normal range by removing the hematoma and decompressive craniectomy (DC), early clipping is often difficult because of higher access difficulty due to brain swelling and high rates of intraoperative rebleeding in high-grade patients[9]. Coiling occludes the ruptured aneurysm in the acute phase without adding additional trauma to the brain, which is less dependent on patient condition, especially in the elderly. With recent technological advances in endovascular treatment, the mortality in high-grade patients with coiling decreased to 24%, compared with 52% previously[2]. Therefore, how to solve the increased ICP due to subarachnoid hematoma and acute hydrocephalus remains the most important part of treatment after aneurysm coiling. DC is adopted as the first

rescue therapy for refractory intracranial hypertension[10-12]. However, several studies have demonstrated that DC is associated with high rates of unfavorable outcomes and death[12-14].

Until now, several authors have reported the usage of external ventricular drainage (EVD) of cerebrospinal fluid and ICP monitoring for controlling ICP in the high-grade patients[15,16]. So far, it is unclear whether EVD and ICP monitoring after coiling could maintain ICP within a normal range and whether they could improve outcomes in high-grade aSAH. We performed a retrospective analysis of patients with high-grade aSAH who were treated with coiling in the acute phase and invasive ventricular ICP monitoring in order to investigate the combination therapy of early coiling and subsequent ventricular intracranial pressure on the outcome of high-grade patients.

MATERIALS AND METHODS

Patients

The retrospective analysis was approved by the research ethics committee of the hospital institution. In all cases, written informed consent was obtained from the patient's legally authorized representative. During the period from January 2016 to June 2017, 182 consecutive patients who presented with an aSAH were treated with coiling in our center. In our center, patients with WFNS grade IV and V were treated routinely with emergent endovascular coiling followed by EVD and invasive ventricular ICP monitoring (Codman MicroSensors ICP Transducer, Codmann). However, those with (1) Large intracerebral or subdural hematoma that would benefit from evacuation; (2) Herniation requiring immediate hemicraniectomy; and (3) Complicated aneurysms were excluded from coiling.

In accordance with the SAH protocol, all patients were admitted to the intensive care unit and were treated. Continuous invasive arterial blood pressure (ABP) monitoring *via* the radial artery and ICP monitoring was performed. The EVD tube was left open with the height levelled at 15 cm above Foramen of Monro for cerebrospinal fluid drainage and control of ICP. CPP was calculated by ABP and ICP and maintained between 60-80 mmHg. For ICP above 20 mmHg, we treated with blood control, analgesia, sedation and osmotherapy (hypertonic saline or mannitol). Additionally, DC was employed for uncontrolled refractory intracranial hypertension.

Data collection

Patients presented with a WFNS IV and V grade and treated in the acute stage (3 d from ictus to coiling) with coiling and ventricular ICP monitoring were included for the current retrospective analysis. Clinical records of neurosurgical examination, interventions and clinical course were collected and evaluated by two independent investigators. Factors in association with outcome were collected for analysis including age, gender, WFNS grade, Glasgow coma scale (GCS), modified Fisher grade, aneurysm site, time interval from ictus to coiling, global brain edema on admission, hydrocephalus, treatment modality, absolute ICP/ CPP repeated measure, rebleeding of aneurysm, EVD related puncture bleeding, delayed cerebral ischemia and intracranial infection. Global brain edema was diagnosed according to the criterion described by Claassen *et al*[17]. Meanwhile, acute hydrocephalus was diagnosed using the age-corrected bicaudate index on the computed tomography scan[18]. Delayed cerebral ischemia (DCI) was diagnosed radiologically when newly developed low-density areas were apparent on postoperative computed tomography.

Outcome assessment

During clinic visits or by telephone interview, survival and functional outcome were assessed using the modified Rankin scale (mRS) score at 6 mo post-hemorrhage. Regarding statistical analysis, outcome was dichotomized into favorable outcome when the mRS score was 0-3 and poor outcome when a score was 4-6.

Statistical analysis

The Fisher exact test was used for analyzing the differences of categorical variables between favorable and poor outcome groups. In addition, the *t* test was also used for continuous variables. Repeated measure analysis of variance was used to assess the relation of absolute ICP/ CPP values repeated measure at different time points with the 6 mo mRS score. The multivariate linear regression was used for factors predicting the functional outcome. Factors with $P \leq 0.2$ in the correlation analysis were included

for multivariate logistic regression. In addition, statistical analysis was performed using IBM SPSS Statistics software Version 19.0 (IBM, Armonk, NY, United States). Significance was set at a probability value lower than 0.05.

RESULTS

Among the 182 patients, 36 patients (19.80%) presented with a WFNS IV and V grade (14 male and 22 females; mean age: 56.85 ± 11.10 years) and were enrolled in the present study (Table 1). No patients suffered from aneurysm re-rupture. With a mean of 7.46 ± 2.54 d, the duration of EVD catheter placement ranged from 3 to 13 d. Seven patients (19.54%) had EVD-related intracranial infection, and fifteen (41.67%) were diagnosed with DCI (Table 2).

The ICP in 33 patients (91.67%) was maintained within the normal range by ICP monitoring during the treatment, and three underwent decompressive hemicraniectomy for uncontrolled aggressive intracranial hypertension. Thirty-two (88.80%) patients survived, and four patients died. Eighteen patients (50.00%) had a favorable outcome.

At baseline, there existed no significant differences in age, gender, WFNS grade, GCS, modified Fisher grade, aneurysm location, hydrocephalus, time interval from ictus to coiling, global brain edema on admission and treatment modality between the favorable outcome group and poor outcome group (Table 1). The continuous variable mRS was significantly correlated with age, GCS and DCI (0.028, 0.040, 0.000, respectively, $P < 0.05$), as shown in Table 3. Multivariate linear regression models showed that DCI and GCS were significant factors in the prediction of 6 mo mRS (2.066 and -0.296, respectively, $P < 0.05$) (Table 4).

DISCUSSION

In this retrospective study, we report the outcomes of patients with high-grade aSAH who were treated by combination therapy of endovascular coiling and invasive ventricular ICP monitoring. Compared to previous studies, in this study, the overall mortality was lower (11.10%), and the 6-mo favorable outcome was slightly higher (50.00%). In this study, intractable ICP was satisfactorily controlled within a normal range in 91.67% of all patients. This finding may suggest that most patients with intractable intracranial hypertension after SAH could be managed using ventricular cerebrospinal fluid drainage, analgesia, sedation, osmotherapy and vasoactive drugs, avoiding DC, which is associated with a high complication rate. The combination therapy of endovascular coiling and ventricular ICP monitoring could also be suitable for high-grade aSAH patients.

Several series of high-grade aSAH patients have been reported to be treated with coiling, which demonstrates that coiling of high-grade ruptured aneurysms is safe and effective and may not be inferior to clipping[12,19-21]. For endovascular coiling, the complete occlusion rate has greatly improved with recent improvements in endovascular techniques and newer-generation endovascular devices. The rebleeding rate after coiling has remarkably decreased, and even complicated wide-neck aneurysms have been successfully treated[2]. In our series, all ruptured aneurysms were successfully embolized with coiling alone or with stent-assisted coiling with no occurrence of aneurysm re-rupture. Several authors have reported higher access difficulty because of brain swelling during early-stage clipping in patients with a poor grade, often requiring excessive retraction or partial lobectomy[9]. The rate of intraoperative aneurysm re-rupture is also higher with clipping, and temporary artery occlusion is often required, which could worsen brain injury[9]. By contrast, coiling adds no extra trauma to the brain. Coiling may be performed at any time, is less dependent on the general patient condition, and is particularly suitable for elderly patients.

Although the value of ICP monitoring in patients with poor-grade aSAH has been questioned[22], our results demonstrated that EVD combined with invasive ICP monitoring was effective in rapidly reducing intracranial hypertension and continuously maintaining ICP within a normal range throughout the treatment. Elevated ICP is a key factor in secondary brain injury in the vicious feed-forward cycle described by Fisher and Oemann[23], and higher ICP is associated with higher mortality rates[22]. Early control of ICP has been reported to be associated with improved outcomes[24]. DC and EVD are commonly used to treat elevated ICP. DC is

Table 1 Demographics and clinical features of high-grade aneurysmal subarachnoid hemorrhage patients

Variables	Overall (n = 36)	Favorable outcome	Poor outcome	P value
		(mRS 0-3) (n = 18)	(mRS 4-6) (n = 18)	
Age in yr	56.83 ± 11.13	54.94 ± 10.52	58.72 ± 11.69	0.315
Gender, male	14 (38.90)	9	5	0.305
Clinical feature				
WFNS grade				1.000
IV	9 (25.00)	4	5	
V	27 (75.00)	14	13	
GCS				0.913
9-12	4 (11.10)	2	2	
6-8	7 (19.40)	3	4	
3-5	25 (69.40)	13	12	
mFisher grade				0.234
1	1 (2.80)	0	1	
2	1 (2.80)	1	0	
3	10 (27.80)	3	7	
4	24 (66.70)	14	10	
Aneurysm site				0.443
Anterior circulation				
AcomA	16 (44.40)	10	6	
PcomA	7 (19.40)	3	4	
ACA	2 (5.60)	1	1	
AchoA	1 (2.80)	0	1	
OphA	1 (2.80)	1	0	
Posterior circulation				
PCA	2 (5.60)	0	2	
BA	1 (2.80)	0	1	
VA	3 (8.30)	1	2	
PICA	3 (8.30)	2	1	
Time interval from ictus to coiling				0.691
< 24 h	28 (80.56)	13	15	
> 24 h, < 72 h	8 (19.44)	5	3	
Global brain edema	26 (72.2)	12	14	0.711
Hydrocephalus	12 (33.3)	5	7	0.725
Treatment modality				1.000
Coiling alone	25 (69.44)	13	12	
Stent-assisted coiling	11 (30.56)	5	6	
Initial ICP	28.09 ± 20.64 mmHg	25.28 ± 16.15 mmHg	31.06 ± 24.70 mmHg	0.416

ACA: Anterior cerebral artery; AchoA: Anterior choroid artery; AComA: Anterior communicating artery; BA: Basilar artery; GCS: Glasgow coma scale; mRS: Modified Rankin scale; ICP: Intracranial pressure; mFisher: Modified Fisher; OphA: Ophthalmic artery; PCA: Posterior cerebral artery; PcomA: Posterior communicating artery; PICA: Posterior inferior cerebellar artery; VA: Vertebral artery; WFNS: World Federation of Neurological Surgeons.

Table 2 Complications in high-grade aneurysmal subarachnoid hemorrhage patients

Complications	<i>n</i> (%), <i>n</i> = 36
Aneurysm re-rupture	0 (0)
Intracranial infection	7 (19.54)
EVD-related puncture bleeding	2 (0.06)
Delayed cerebral ischemia	15 (41.67)
Decompressive hemicraniectomy	3 (8.83)
Ventriculoperitoneal shunt	7 (19.54)

EVD: External ventricular drainage.

Table 3 Correlation between clinical features and 6 mo modified Rankin scale score

Clinical features	mRS score	
	CC	<i>P</i> value
Age	0.367	0.028 ^a
Gender	0.180	0.294
WFNS grade	0.037	0.930
GCS	-0.344	0.040 ^a
mFisher grade	-0.230	0.176
Time interval from ictus to coiling	-0.021	0.902
Global brain edema	0.200	0.242
Hydrocephalus	0.054	0.753
Delayed cerebral infarct	0.622	0.000 ^a

^a*P* < 0.05. CC: Correlation coefficient; GCS: Glasgow Coma scale; mFisher: Modified Fisher; mRS: Modified Rankin scale; WFNS: World Federation of Neurological Surgeons.

Table 4 Multivariate linear regression of 6-mo modified Rankin scale

Variables	b (95%CI)	<i>P</i> value
Age	0.32 (-0.018, 0.083)	0.199
GCS	-0.296 (-0.583, -0.195)	0.043 ^a
mFisher grade	-0.652 (-1.499, 0.195)	0.127
Delayed cerebral ischemia	2.066 (0.780, 3.352)	0.003 ^a

^a*P* < 0.05. Glasgow coma scale and delayed cerebral ischemia are significant predictors of functional outcome. CI: Confidence interval; GCS: Glasgow Coma scale; mFisher: Modified Fisher.

effective in reducing ICP and increasing CPP[12,25]. This procedure is preferred by neurosurgeons, as it can be performed immediately after clipping ruptured aneurysms. However, DC is associated with high complications and poor outcomes with high mortality[12,13]. For high-grade patients without a mass effect or herniation, there remains considerable controversy regarding the standard criteria for performing DC and whether DC significantly improves the outcome[12,26]. Some authors have recommended EVD, instead of DC, for increased ICP because of EVD effectiveness in ICP control[27]. Our results also supported this suggestion. In our study, intractable ICP was satisfactorily controlled within a normal range in 91.67% of the patients throughout the treatment.

Most importantly, continuous ICP monitoring allows early detection of potentially harmful events before they have caused irreversible damage. For example, such monitoring helps determine whether a ventriculoperitoneal shunt is required after withdrawal of EVD. In addition, continuous ICP monitoring and ABP monitoring afford several parameters, such as the ICP wave and pressure reactivity index (PRx, an index for cerebrovascular autoregulation), for the clinical assessment of neurological deterioration changes in comatose or sedated patients. Another benefit of ICP monitoring is that real-time CPP could be calculated from real-time ICP and ABP, which could facilitate clinical CPP-targeted therapy. Impaired cerebral autoregulation and decreased intracranial compliance were often observed in high-grade patients. This suggests that both low CPP and high CPP are harmful to the injured brain, resulting in ischemia or hyperemia, respectively. With ICP monitoring, controlled ICP and optimal CPP therapy are possible.

There are nevertheless some limitations: (1) This was a retrospective study, and some factors may have influenced the results; and (2) The sample size was relatively small. Larger, well-designed prospective randomized clinical trials are needed to validate this treatment strategy for high-grade aSAH patients.

CONCLUSION

In conclusion, intractable intracranial hypertension in high-grade aSAH patients could be managed through EVD and ICP monitoring. Combination therapy of early endovascular coiling, followed by EVD and ICP monitoring, may also be suitable for high-grade aSAH patients.

ARTICLE HIGHLIGHTS

Research background

High-grade aneurysmal subarachnoid hemorrhage (aSAH) is a devastating disease with high mortality and a low favorable outcome. Elevated intracranial pressure (ICP) is a substantial feature of high-grade aSAH that can result in secondary brain injury. Early control of ICP including decompressive craniectomy and external ventricular drainage (EVD) had been reported to be associated with improved outcome. In recent years, several studies had been reported that coiling of high-grade aSAH is safe and effective and may not be inferior to clipping. However, little is known whether EVD and ICP monitoring after coiling could improve outcome in high-grade aSAH.

Research motivation

A retrospective analysis of patients with high-grade aSAH who were treated with coiling in the acute phase and invasive ventricular ICP monitoring to investigate the combination therapy of early coiling and subsequent ventricular intracranial pressure on the outcome of high-grade patients. This research will demonstrate the value of ICP monitoring during the therapy for high-grade aSAH patients. This result will suggest that continuous ICP monitoring and targeted therapy may be beneficial for high-grade aSAH patients.

Research objectives

High-grade patients without (1) Large intracerebral or subdural hematoma that would benefit from evacuation; (2) Herniation requiring immediate hemicraniectomy; and (3) Complicated aneurysms were included for the study. They received emergent endovascular coiling followed by invasive EVD with ventricular ICP monitoring. The authors investigated the overall survival and functional outcome. The desired results of decreased mortality would suggest that high-grade patients would benefit from endovascular coiling combined with EVD and ICP monitoring. For future research, the authors need to further understand the effects of ICP fluctuations on the prognosis of patients and to clarify whether individual cerebral perfusion pressure (CPP) targeted therapy could improve the prognosis of high-grade patients.

Research methods

Patients presented with a World Federation of Neurological Surgeons IV and V grade and treated in the acute stage (3 d from ictus to coiling) with coiling and ventricular

ICP monitoring were included for this retrospective analysis. Factors related to outcome were collected for analysis including age, gender, World Federation of Neurological Surgeons grade, Glasgow coma scale, modified Fisher grade, aneurysm site, time interval from ictus to coiling, global brain edema on admission, hydrocephalus, treatment modality, absolute ICP/ CPP repeated measure, rebleeding of aneurysm, EVD related puncture bleeding, delayed cerebral ischemia and intracranial infection. Survival and functional outcome [modified Rankin scale (mRS)] were assessed. The Fisher exact test was used for analyzing the differences of categorical variables between favorable (mRS 0-3) and poor outcome (mRS 4-6) groups, and the *t* test was used for continuous variables. Repeated measure analysis of variance was used to assess the relation of absolute ICP/ CPP values repeated measured at different time point with the 6 mo mRS score. The multivariate linear regression was used for factors predicting the functional outcome. Factors with $P \leq 0.2$ in the correlation analysis were included for multivariate logistic regression. Significance was set at a probability value lower than 0.05.

Research results

Thirty-two (88.80%) patients survived while four died. Eighteen patients (50.00%) had a favorable outcome during follow-up. Seven patients (19.54%) had EVD-related intracranial infection. Multivariate linear regression models showed that delayed cerebral infarct and Glasgow coma scale were significant factors in predicting 6 mo mRS. Compared to the previous similar studies, the overall mortality (11.10%) was lower, and the 6 mo favorable outcome (50.00%) was slightly higher in this study. The results also demonstrated that EVD combined with invasive ICP monitoring was effective in improving the prognosis of high-grade patients.

Research conclusions

Intractable intracranial hypertension in high-grade aSAH patients could be managed through EVD and ICP monitoring. Combination therapy of early endovascular coiling followed by EVD and ICP monitoring may improve the prognosis of high-grade aSAH patients. Stabilization of intracranial pressure in a normal range after endovascular coiling may improve the prognosis of high-grade aSAH patients. Combination therapy of early endovascular coiling followed by EVD and ICP monitoring may improve the prognosis of high-grade aSAH patients. Patients should receive microsurgical aneurysm clipping and decompressive craniectomy. Coiling adds no additional trauma to the brain compared with clipping. EVD and ICP monitoring is not inferior to the decompressive craniectomy in controlling and stabilizing ICP. Combination therapy of early endovascular coiling followed by EVD and ICP monitoring may improve the prognosis of high-grade aSAH patients. Patients with high-grade aSAH received emergent endovascular coiling except for (1) Large intracerebral or subdural hematoma that would benefit from evacuation; (2) Herniation requiring immediate hemicraniectomy; and (3) Complicated aneurysms. After coiling, invasive external ventricular drainage with ventricular ICP monitoring were undertaken. Continuous invasive arterial blood pressure (ABP) monitoring *via* the radial artery. CPP was calculated by ABP and ICP and maintained between 60-80 mmHg during the therapy. This study demonstrated a decreased overall mortality (11.10%) and improved 6 mo favorable outcome (50.00%) compared to previous studies. Increased ICP could be stabilized and maintained within the normal range by ICP monitoring in 91.67% of the patients. Combination therapy of early endovascular coiling followed by EVD and ICP monitoring may improve the prognosis of high-grade aSAH patients. EVD and ICP could also stabilize and maintain ICP within the normal range compared with decompressive craniectomy, which is more traumatic. Early endovascular coiling followed by EVD and ICP monitoring may be more suitable for high-grade aSAH patients.

Research perspectives

The sample size of this study is small, so in the future study, the sample size needs to be increased. Also, it is necessary to monitor cerebral blood flow monitoring using transcranial Doppler to obtain the cerebral blood flow value for each patient. In the future research, the damage of autoregulatory function of cerebral blood vessels should be studied through intracranial pressure monitoring in high-grade aSAH patients. The future study should also focus on the impact of optimal CPP targeted therapy on patient prognosis. The best research in the future is a clinical comparative study of surgical clipping combined with decompressive craniectomy and endovascular coiling combined with ventricular ICP monitoring.

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